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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,216	09/19/2003	Shaker A. Mousa	2747/1021	7027

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EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 03/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/667,216	MOUSA, SHAKER A.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-44 and 47-60* is/are pending in the application.

4a) Of the above claim(s) *6-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,43,44 and 47-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's amendments and remarks filed on 08/31/2005 are acknowledged. Claims 3-4 and 45-46 have been cancelled and replaced by new claims 55-60. Claims 1, 2, 43, 44 and 47 have been amended. Claims 6-42 have been withdrawn previously.

Claims 1,2,5,43,44 and 47-60 are currently pending in this application.

35 U.S.C. 112, second paragraph rejection

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,2,5,43,44 and 47-60 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A) The terms "substantially" and "sufficient to substantially", in amended claims 1 and 43 are relative terms, which render the claims indefinite. The terms "substantially" and "sufficient to substantially", are not defined in relation to the claimed composition, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(B) The term "analogs" is a relative term, which renders the claim 54 indefinite. In the absence of the specific functional group to the compound or analogs claimed core or

distinct language to describe the structural modifications or the chemical names of analogs claimed, the identity of said analogs would be difficult to describe and the metes and bounds of said analog applicants regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claim.

Claims which depend from an indefinite claim which fail to obviate the indefiniteness of the claim from which they depend are also seen to be indefinite and are also rejected for the reasons of record.

Rejection Maintained

Rejection of claim 54 under 35 U.S.C. 112, second paragraph, is maintained for the reasons of record.

Response to Arguments

Applicant's arguments filed on 8/31/2005 traversing the rejection of claim 54 under 35 U.S.C. 112, second paragraph have been fully considered but they are not persuasive. Applicant has not addressed the chemical name, structural formula or sufficiently distinct functional language, the particular moieties applicant regards as those which will facilitate modification, requisite to identifying the compound of matter claimed. Applicants argue, "one skilled in the art would have no difficulty ascertaining which compounds were encompassed by the term "analog"". The skilled artisan knows analog means chemical molecules, which differ only by the transposition of one atom or a

simple functional group for another. Applicant's claims fail to particularly point out such atom or functional group. Metes and bounds of the atom or functional group applicant intends can not be readily ascertained. The presence of the terms "analog" in other document is noted. It is the deficiency in this application, which is at issue.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1,2,5,43,44, 47-54 and newly added claims 55-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mascellani et al. (Mascellani) (U.S. Patent 4,973,580) in view of Cohen et al. (Cohen) (U.S. Patent 5,908,837) of record.

Mascellani discloses the depolymerized or oxidized heparins, heparin sulfate, dermatan sulfates and chondroitin sulfates (abstract). Mascellani discloses the oxidizing process of heparin with periodate to produce a reduced molecular weight product and a pharmaceutical composition thereof having a high antithrombotic activity, poor or no anticoagulant activity, a high fibrinolytic activity and an anti-inflammatory activity with a good bioavailabilty (col. 1, lines 15-25). Mascellani is silent in disclosing the oxidized percent range of the oxidized hydroxyl groups by the said process. Mascellani discloses the said heparin with a low molecular weight ranging between 2000-7000 (col. 4, lines

55-60). Mascellani also discloses the sulfate to carboxylate ratio between >2: 1 (col. 6, Table 1). Mascellani discloses that the oxidation process does not change the sulfate content of heparin, which is important for the biological activity (col. 4, lines 35-40). Mascellani discloses the good bioavailability of said reduced molecular weight fractions after oral administration (col.1,line 25); although the prior art is silent in disclosing the sustained release of said fraction however it will be obvious to one skilled in this art to use said fraction to accomplish the sustained release of the heparin fraction. Furthermore, Mascellani discloses the pharmaceutical compositions for parenteral, topical and oral administration (col.4, lines 60-65); the encapsulated forms such as tablet and capsule are disclosed (col.5, line 5.

Mascellani differs from the applicant's invention that Mascellani does not provide an explicit example of a composition containing a heparin fraction in combination with a non-heparin agent or drug.

Cohen teaches the use of low molecular weight heparins in a pharmaceutical composition in combination with a non-heparin angiogenesis inhibitor (col.3, lines 50-60). Cohen discloses periodate oxidized heparins having a low molecular weight between 3000-6000, a pharmaceutical composition containing a pharmaceutical carrier (col. 4, lines 10-45). Cohen also discloses that the combination of the heparin and a non-heparin agent is more effective in the inhibition of angiogenesis (col. 3, lines 57-58). Therefore applicant's use of a non-heparin anticoagulant or a cytotoxic or chemotherapeutic agent in combination with the low molecular weight oxidized heparin fraction are obvious over the prior art.

It would have been obvious to person having ordinary skill in the art at the time the invention was made, to select heparin fraction or a composition thereof consisting of constituents having molecular weight between 2,000-4,000 daltons in combination with a non-heparin agent or drug, from among those taught by Mascellani and Cohen, because Mascellani discloses oxidized heparin with a low molecular weight ranging between 2000-7000 and Cohen teaches the use of low molecular weight heparins in a pharmaceutical composition in combination with a non-heparin angiogenesis inhibitor. Mascellani the motivation to use oxidized low molecular weight heparin fraction and a pharmaceutical composition thereof due to their high antithrombotic activity, poor or no anticoagulant activity, a high fibrinolytic activity and an anti-inflammatory activity with a good bioavailabilty (sustained release) (col. 1, lines 15-25).

Response to Arguments

Applicants' arguments traversing the rejection of claims 1,2,5,43,44 and 47-60 under 35 U.S.C 103(a) have been fully considered but they are not persuasive.

Applicants argue, Mascellini and Cohen "does not disclose a heparin fraction in which anticoagulant activity has been substantially eliminated nor a heparin fraction in which the hydroxyl residues are oxidized in an amount sufficient to substantially eliminate anticoagulant activity".

Mascellani discloses oxidized heparin with a low molecular weight ranging between 2000-7000 and Cohen teaches the use of low molecular weight heparins in a

pharmaceutical composition in combination with a non-heparin angiogenesis inhibitor. In the instant case, the use of oxidized low molecular weight heparins in a pharmaceutical composition would be considered an inherent property which can be used to produce a composition for sustained release comprising oxidized heparin with a low molecular weight ranging between 2000-7000, absent any clear and convincing evidence and/or arguments to the contrary.

The patentability of a product does not depend on its method of production or its use. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe,* 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

2. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang, Supervisory Patent Examiner, Art Unit 1623 can be reached at (571)272-0627. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,J.D.
Art Unit 1623
March 6, 2006

3/6/06

Anna Jiang, Ph.D.
Supervisory Patent Examiner
Technology Center 1600